REMARKS

Claims 1, 2, 3, 6, 8, 22, 57 are currently amended. Claims 59-63 are canceled. Claims 4, 5, 7, 9, 11, 13 and 58 are withdraw-currently amended. Claims 64-82 are new. No new matter is added. Reconsideration of the pending claims is requested in light of the amendments above and remarks below.

I: The Sequence Listing

Please enter the new sequence listing as directed above. Applicants note that the prior pending sequence listing was incorrect with respect to SEQ ID NO:28. No new matter has been added and the Examiner is directed to page 66 of the application for support. In other words, the sequence listing does not include any new matter that goes beyond the disclosure of the application as filed. Applicants have submitted the new sequence by EFS-Web. A paper copy is also included. The electronic copy and the paper copy is the same.

II: The restriction requirement

The Examiner has erred by withdrawing claims 4, 5, 7, 9, 11 and 58. The Examiner has erred applying the rationale that if, on examination of an elected species, it is found to be anticipated or rendered obvious by prior art, the Markush type claim and claims to the elected species shall be rejected, and claims to non-elected species shall be withdrawn.

This rationale is wrong for three reasons. First, a Markush type claim includes the language "selected from the group consisting of . . .. and . . .". While Claim 1 includes alternative claim language it is not a Markush claim. Second, for the reasons stated below in section (IV), Tang is not suitable prior art and does not anticipate or make obvious the invention because Tang does not enable the claimed invention. Third, the sequence MKWVFIVSILFLFSSAYS is SEQ ID NO:28, the elected species. See page 66 in the application. It is inappropriate to withdraw the species that was specifically identified as the elected species.

Accordingly, it is improper to withdraw these claims from consideration. Reconsideration is urged.

III: The rejection of Claims 1 and 21-25 under 35 U.S.C. 101

Claim 1 is currently amended to relate to a non-naturally occurring polypeptide. Reconsideration is urged.

IV: The rejection of Claims 1-3, 8, 20-22, 24 and 57 under 35 U.S.C. 102(b)

Claims 1-3, 8, 20-22, 24 and 57 stand rejected under 35 U.S.C. 102(b) as anticipated by WO 01/64834 (hereinafter referred to simply as "Tang").

Independent Claims 1 and 57, as currently amended, require, *inter alia*, an albumin secretion pre sequence or albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28. Nowhere does Tang disclose an albumin secretion pre sequence in accordance with Claims 1 and 57. Accordingly, Tang does not anticipate the claimed invention. Reconsideration is urged.

Further, Tang is not an enabling prior art reference, thus is not suitable as a reference under 35 U.S.C. 102(b). ("[A] prior art reference must be enabling so that the claimed subject matter may be made or used by one skilled in the art."); *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1374 (Fed. Cir. 2001) ("To anticipate, the reference must also enable one of skill in the art to make and use the claimed invention."). Here, Tang discloses SEQ ID NO: 589 (cited by the Examiner), however the reference is deficient in describing an albumin secretion pre sequence, thus does not enable the claimed invention. Reconsideration is urged.

Applicants note that the use of the term "comprising" does not fail independent claims 1 and 57 as alleged by the Examiner. The Examiner is incorrect that the use of the term "comprising" allows for an unlimited number of amino acids to be present in a polypeptide and that the presence of the motif in SEQ ID NO:589 of the cited reference anticipates limitations of claim 57. The term "comprising" is well established and understood, and does not in itself fail Claims 1 or 57. "Comprising" when used in claim language, means "the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." *Genentech, Inc. v. Chiron Corp.*, 42 USPQ2d 1608 (Fed. Cir. 1997). "For example, a pencil structurally infringing a patent claim would not become noninfringing when incorporated into a complex machine that limits or controls what the pencil can write. Neither would infringement be negated simply because the patentee failed to contemplate use of the pencil in that environment." *A.B. Dick Co. v. Burroughs Corp.*, 218 USPQ 965 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1042 (1984). Tang is deficient because it does not disclose an albumin secretion pre sequence and because it is not an enabling reference. The Office cannot ignore claim features, such as albumin secretion pre sequence in its analysis. Claims 1 and 57 are not anticipated. Reconsideration is urged.

Applicants note that dependent Claims 2, 3, 8, 20-22, 24 are not anticipated for the same reasons claims 1 and 57 are not anticipated. Reconsideration is urged.

V: The rejection of Claims 1-3, 8, 10, 20-25 and 57 under 35 U.S.C. 112, 1st paragraph

Claims 1-3, 8, 10 and 20-25 and 57 stand rejected under 35 U.S.C. 112, 1st paragraph. The Examiner states, *inter alia*, the claim does not recite the nature of the 'leader sequence', 'pre-sequence' or 'the mature desired protein' in terms of the amino acid sequences that would properly define each of these different peptides that constitute the claimed polypeptide sequence. Initially, Independent claims 1 and 57 have been amended to refer to an albumin secretion pre sequence or albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28. Thus, Applicants have been completely responsive to the Examiner's rejection. Consideration of the amendments above is requested.

Notwithstanding the above amendments, Claims 1 and 57, as amended, meet the written description standard.

Section 112 of Title 35 provides, in relevant part, that:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. §112, ¶1 (emphasis added). The emphasized portion of §112, the written description requirement, "serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

The written description requirement of 35 U.S.C. § 112, first paragraph, is fulfilled when the patent specification describes the claimed invention in sufficient detail such that the claim limitations are described so that one of skill in the art would recognize that the applicants had invented the subject matter. See *Vas-Cath, Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); *In re Herschler*, 591. F.2d 693, 700 (C.C.P.A. 1979). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See *In re Marzocchi*, 169 U.S.P.Q. 367 (CCPA 1971).

The written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. See, e.g., *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997); *Enzo Biochem v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002). A description of a claimed genus may be achieved by recitation of a representative number of species falling within the scope of the genus or by a recitation of structural features common to the members of the genus which constitute a substantial portion of the genus. See *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d at 1569.

The Patent Office's *Written Description Training Materials*, Revision 1, (March 25, 2008), also provides guidance as to how to determine if there is sufficient written description to inform the artisan that the applicant was in possession of the claimed genus at the time the application was filed. These guidelines instruct that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. For example, the Written Description Guidelines expressly state "The number of species required to represent a genus will vary, depending on the level of skill and knowledge in the art and the variability among the claimed genus. For instance, fewer species will be required where the skill and knowledge in the art is high, and more species will be required where the claimed genus is highly variable." See pages 1-2. Further, the Examples in the Guidelines support that the written description requirement for a claimed genus may be satisfied through sufficient description in the specification of function of the described molecule which is correlated to its structure. *See* Example for Claim 4, pages 52-53.

"To satisfy the written description requirement, "the applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *Carnegie Mellon Univ. v. Hoffmann La Roche Inc.,* 541 F.3d 1115, 1122 (Fed. Cir. 2008) (quoting *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996)). "In other words, the applicant must 'convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention,' and demonstrate that by disclosure in the specification of the patent." Id. (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991)). Such disclosure need not recite the claimed invention *in haec verbal*, but it must do more than merely disclose that which would render the claimed invention obvious. *Rochester*, 358 F.3d at 923; *Regents of the Univ. of Cal. V. Eli Lilly & Co.*, 119 F.3d 1559,

1566-67 (Fed. Cir. 1997); *see also PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1306-07 (Fed. Cir. 2008) (explaining that §112 ¶1 "requires that the written description actually or inherently disclose the claim element").

"Whether the written description requirement is satisfied is a fact-based inquiry that will depend on the nature of the claimed invention and the knowledge of one skilled in the art at the time an invention is made and a patent application is filed." *Carnegie Mellon*, 541 F.3d at 1122 (citing *Enzo*, 323 F.3d at 963). The written description requirement is not satisfied by :[t]he appearance of mere indistinct words in a specification or a claim, even an original claim . . . A description of what a material does, rather than of what it is, usually does not suffice." *Enzo*, 323 F.3d at 968 (citing *Eli Lilly*, 119 F.3d at 1568); *see Rochester*, 358 F.3d at 926 ("[G]eneralized language may not suffice if it does not convey the detailed identity of an invention.").

Of course, what is adequate depends upon the context of the claimed invention. *See Capon*, 418 F.3d at 1358 ("The written description requirement must be applied in the context of the particular invention and state of the knowledge."). The Court of Appeals for the Federal Circuit has articulated a variety of factors to evaluate the adequacy of the disclosure supporting "generic claims to biological subject matter." Id. at 1359. These factors include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Id.*

The present invention is enabled. In the field of molecular biology, the level of skill in this art is high.

Under this standard, the Examiner's conclusion that the specification requires more to meet the written description standard is plainly incorrect. This is not a case where the specification is deficient and vaguely states what a material does. Conversely, the specification is very detailed and explains what a leader sequence, an albumin secretion pre sequence or albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28, and the sequence of mature desired proteins are. Accordingly, the specification discloses, and one skilled in the art would clearly recognize that the scope of the present invention includes a leader sequence, an albumin secretion pre sequence or albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28, and the sequence of mature desired protein.

For example, albumin secretion pre sequences and variants thereof are clearly described on, *inter alia*, pages 18-19. Here, the specification clearly explains that, in embodiments, the leader sequence of a polypeptide includes a secretion pre sequence derived from albumin secretion pre sequence, or variant thereof. Variant of albumin pre sequence is

specifically defined on page 19, lines 5-9. Various examples are provided on, *inter alia*, pages 19-23. Importantly, Fig. 1 shows a modified leader sequence of the present disclosure (third line) including an embodiment of an albumin secretion pre sequence. Further, the examples conclude that the introduction of the polypeptide sequence according to the present invention led to a significant improvement in the production of the desired polypeptide.

Albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28 fall within the scope of the claimed invention. For example, variant of an albumin pre sequence refers to albumin pre sequence wherein at one or more positions, other than a those defined by as X1-X5, include amino acid insertions, deletions, or substitutions, either conservative or non-conservative, provided that the changes still allow the peptide to act as a pre sequence. Importantly, the specification defines conservative substitution on page 9. Further "variant" of an albumin pre sequence has been clearly described as having, other than the residues defined as X1-X5, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 identical amino acids to a naturally occurring albumin pre sequence, including the albumin sequence of Fig. 1. See page 19. Clearly, 60% sequence identity is clearly envisioned by an artisan once apprised of Applicants' invention. See for example page 19 as described above.

Accordingly, an artisan would reasonably conclude that Applicants were not only in possession of albumin pre sequence such as the one disclosed in Fig. 1, but also that Applicants had possession of highly related sequences, as specified by the claims. Indeed, based on the high level of skill in the art, the examples and direction on page 19 convey to the artisan that Applicants were in possession of the claimed invention.

Notwithstanding the above, the Examiner has not provided sufficient evidence or reasoning to rebut that the specification provides an adequate written description for highly related albumin pre sequence as claimed. In this regard no additional representative species are required to be disclosed. Given the high level of skill in the art and high degree of identity recited in the claims, an extremely high degree of predictability exists as to the structure and function of sequences falling within the claims.

Applicants note that the Examiner interview dated 28 October 2008 indicates that incorporating limitations of claim 11 into claim 1 would have placed the application in condition for allowance. As Claim 11 relates only to the pre sequence, Applicants understand that the claim language relating to leader sequence and desired proteins is admitted to be in the possession of Applicants.

Notwithstanding this understanding, sequences of mature desired proteins are clearly described on page 8, at line 4-7, further including all references to desired proteins which were

known in the art. See for example, page 8, line 8 through page 13 line 8 describing in great detail desired proteins in accordance with the present disclosure. This detailed section defines variants and fragments of the desired proteins and variants thereof. This detailed section includes methodology routine in the art for comparing sequences, for example measuring percent identity and making alignments.

Moreover, leader sequence is described on, *inter alia*, pages 13, lines 20 through page 24, line 25. This detailed section describes a leader sequence including, in embodiments, leader sequence characterized in that it includes a secretion pre sequence that includes a motif. This section further describes secretion leader sequence and explains that a sequence acts as a secretion leader sequence if, in comparison to an equivalent polypeptide without the secretion pre sequence, it causes more of that polypeptide to be secreted from the host cell in which it is produced. Further, a test is described where one can measure whether a given sequence is able to achieve a given level of secretion (see pages 15 -18). The description also explains that in embodiments, the leader sequence is derived from immature version of the mature protein to which it is, or is intended to be attached. Importantly, Fig. 1 shows a modified leader sequence of the present disclosure (third line). Further, the examples conclude that the introduction of the polypeptide sequence according to the present invention led to a significant improvement in the production of the desired polypeptide.

For the foregoing reasons, Applicants respectfully submit that the specification contains a sufficient description of the structural and functional characteristics of the claimed sequences to fulfill the requirements of 35 U.S.C. 112. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

VI: The rejection of Claims 59-63 under 35 U.S.C. 112, 1st paragraph (New Matter)

Claims 59-63 are canceled and the rejection is moot.

VII: The rejection of claims 1, 6, 8, 20-22, 24 and 57 under 35 U.S.C. 102(b)

Claims 1, 6, 8, 20-22, 24 and 57 stand rejected under 35 U.S.C. 102(b) as being anticipated by Street, 1996, Biochimica et Biophysica Acta, 1305, 87-97 (hereinafter referred to simply as "Street").

Independent Claims 1 and 57, as currently amended, require, *inter alia*, an albumin secretion pre sequence or albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28. Nowhere does Street disclose an albumin secretion pre sequence in

accordance with Claims 1 and 57. Accordingly, Street does not anticipate the claimed invention. Reconsideration is urged.

The claims that depend from claims 1 and 57 are not anticipated for the same reasons.

VIII: The rejection of claims 1, 2, 4, 6, 8, 20-22, 24 and 57 under 35 U.S.C. 102(b)

Claims 1, 2, 4, 6, 8, 20-22, 24 and 57 stand rejected under 35 U.S.C. 102(b) as being anticipated by Munson, 1993, Journal of Bacteriology, 175, 6426-6432 (hereinafter referred to simply as "Munson").

Independent Claims 1 and 57, as currently amended, require, *inter alia*, an albumin secretion pre sequence or albumin secretion pre sequence having 60% sequence identity to SEQ ID NO:28. Nowhere does Munson disclose an albumin secretion pre sequence in accordance with Claims 1 and 57. Accordingly, Munson does not anticipate the claimed invention. Reconsideration is urged.

The claims that depend from claims 1 and 57 are not anticipated for the same reasons.

IX. New Claims

New claims 64-82 are added. No new matter is added. Should any additional fees be due, the USPTO is authorized to charge the deposit account of Novozymes North America, Inc., *i.e.*, deposit account no. 50-1701.

X. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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